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EXAMINER	
FORMAN, BETTY J	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 12/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/721,550	REICH, NORBERT	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-7,10-18,20,23,25,29,31,34,35 and 37-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-7,10-18,20,23,25,29,31,34,35 and 37-40* is/are rejected.

7)☒ Claim(s) *6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☒ Interview Summary (PTO-413) Paper No(s). *9/03*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

1. This action is in response to papers filed 29 September 2003 in which the specification was amended to cross-reference provisional application 60/167,421 and Claims 28 and 32 were canceled. The amendments has been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 16 June 2003 are withdrawn in view of the amendment to the specification wherein priority to the provisional application is claimed.

New grounds for rejection necessitated by the amendment are discussed.

Claims 1, 4-7, 10-18, 20, 23, 25, 29, 31, 34-35, 37-40 are under prosecution.

Priority

2. Applicant's claim for domestic priority under 35 U.S.C. 119 is acknowledged.

Specification

3. The amendment filed 29 September 2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

The amendment recites that the provisional application 60/167,421 is "herein incorporated by reference in its entirety". The incorporation by reference statement added by amendment to the specification is deemed new matter (see MPEP § 201.06(c).).

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Objections

4. Claim 6 is objected to because of the following informalities:

In papers filed 14 January 2003, Claim 6 was amended to depend from Claim 1. However, the amendment of 14 January 2003 is not reflected in Claim 6 as currently written. As written, Claim 6 incorrectly depends from canceled Claim 2.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1, 4, 7, 23, 25, 29, 31 and 38 are rejected under 35 U.S.C. 102(e) and (a) as being anticipated by Wu et al (U.S. Patent No. 5,846,729, issued 8 December 1998).

Regarding Claim 1, Wu et al disclose a substrate having a surface area comprising attached labeled probe molecules, said labeled probes having incorporated therein nucleotide analogs that fluoresce (Column 4, lines 28-45) and whose decrease in fluorescence quantifies the presence or hybridization of complementary molecules by quenching a first fluorescence provided by the labeled probes (Column 4, lines 45-61 and Column 8, lines 7-19).

Regarding Claim 4, Wu et al disclose the substrate wherein the probes are comprised of native and non-native probes i.e. DNA or RNA (native) and wherein the probes incorporate analogs (non-native) (Column 3, lines 22-27 and Column 4, lines 28-45).

Regarding Claim 7, Wu et al disclose the substrate wherein the probes are comprised of amino acids i.e. PNA (Column 4, lines 4-44).

Regarding Claim 23, Wu et al disclose a method for monitoring the hybridization of target and probe comprising, providing a fluorescently labeled probe said probe being fluorescence due to the incorporation of at least one nucleotide analog thereby providing a detectable first level of fluorescence and providing a second level of fluorescence when hybridized to a complementary unlabeled target wherein the second level is significantly lower than the first level and approaching zero i.e. quenching (Example 1; Example 5A; and Fig. 6).

Regarding Claim 25, Wu et al disclose a method for monitoring the hybridization of target and probe comprising, supplying a fluorescently labeled probe said probe being fluorescence due to the incorporation of at least one nucleotide analog thereby providing a detectable first level of fluorescence and providing a second level of fluorescence when

hybridized to a complementary unlabeled target wherein the second level is significantly lower than the first level and approaching zero i.e. quenching and utilizing the reduced fluorescence to quantify unlabeled target (Column 4, lines 51-61; Example 5A; and Fig. 6).

Regarding Claim 29, Wu et al disclose a substrate having a known and quantified plurality of probes (Column 7, lines 25-40) wherein said probes are fluorescently labeled by incorporation of at least one nucleotide analog (Column 4, lines 28-61) the labeled probe providing a first level of fluorescence and when hybridized to a complementary target having no analogs providing a second level of fluorescence and wherein the known and quantified probes provides for quantification of the target (Column 4, lines 28-61 and Column 8, lines 7-19).

Regarding Claim 31, Wu et al disclose a substrate having a surface area comprising attached quantified labeled probes, said probes further comprising a fluorescent label including at least one nucleotide analog incorporated as part of the sequence defining the probe (Column 4, lines 28-61 and Column 8, lines 7-19).

Regarding Claim 38, Wu et al disclose the substrate of Claim 1 wherein the probe fluoresces at a wavelength of about 300nm to about 700nm (Column 6, lines 30-41).

7. Claims 5, 6, 34, 35, 37 and 39 are rejected under 35 U.S.C. 102(e) and (a) as being anticipated by Wu et al (U.S. Patent No. 5,846,729, issued 8 December 1998) as defined by Egholm et al (Nature, 7 October 1993, 365: 566-568).

Regarding Claims 5, 6 and 39, Wu et al disclose the substrate of Claim 1 having a surface area comprising attached labeled probe molecules, said labeled probes having

incorporated therein nucleotide analogs that fluoresce (Column 4, lines 28-45) and whose decrease in fluorescence quantifies the presence or hybridization of complementary molecules by quenching a first fluorescence provided by the labeled probes (Column 4, lines 45-61 and Column 8, lines 7-19). Furthermore, they teach the probes comprise PNA nucleotide analogs as described by Egholm et al (Column 4, lines 19-25). Egholm teaches that PNA nucleotide analogs are 2-amino purine (Abstract). Therefore, the PNA nucleotide analogs of Wu et al are 2-amino purines as claimed.

Regarding Claims 34 and 35, Wu et al disclose a substrate having a surface area comprising attached quantified labeled probes, said probes further comprising a fluorescent label including at least one nucleotide analog incorporated as part of the sequence defining the probe (Column 4, lines 28-61 and Column 8, lines 7-19). Furthermore, they teach the probes comprise PNA nucleotide analogs as described by Egholm et al (Column 4, lines 19-25). Egholm teaches that PNA nucleotide analogs are 2-amino purine (Abstract). Therefore, the PNA nucleotide analogs of Wu et al are 2-amino purines as claimed.

Regarding Claim 37, Wu et al disclose a method for quantifying the amount of a target comprising incorporating a nucleotide analogue into a probe (Column 4, lines 28-61), affixing the probe on a substrate, detecting a first level of fluorescence, contacting the substrate with a volume of sample containing unlabeled target molecules, providing hybridization conditions, removing the substrate and detecting the second level of fluorescence, comparing the first and second levels of fluorescence and identifying probe-target hybridization as the level of fluorescence approaches zero i.e. decreases by quenching (Column 7, lines 23-41 and Column 8, lines 8-19).

Furthermore, they teach the probes comprise PNA nucleotide analogs as described by Egholm et al (Column 4, lines 19-25). Egholm teaches that PNA nucleotide analogs are 2-amino purine (Abstract). Therefore, the PNA nucleotide analogs of Wu et al are 2-amino purines as claimed.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 10-13, 16-17 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al U.S. Patent No. 5,846,729, issued 8 December 1998) in view of McGall et al (U.S. Patent No. 6,156,501, filed 3 April 1996).

Regarding Claims 10-13, Wu et al disclose the substrate of Claim 1 having a surface area comprising attached labeled probe molecules, said labeled probes having incorporated therein nucleotide analogs that fluoresce (Column 4, lines 28-45) and whose decrease in fluorescence quantifies the presence or hybridization of complementary molecules by quenching a first fluorescence provided by the labeled probes (Column 4, lines 45-61 and Column 8, lines 7-19). Wu et al teach the substrate is a solid support (Column 8, line 7) but they are silent regarding the support being a microarray divided into quadrants (Claim 10); having about 100 to 10,000 different probes on about 100 to 10,000 different quadrants (Claim 11); having about 10 to 1,000 different probes per quadrant (Claim 12); and wherein the substrate is a bead (Claim 13).

However, bead substrates and microarrays having the claimed probes and quadrants were well known in the art at the time the claimed invention was made as taught by McGall et al. Specifically, McGall et al teach bead and microarray substrates (Column 2, lines 5-8) comprising about 10 to about 1,000 different probes comprising analogs on about 100 to about 10,000 different quadrants (Column 1, line 59-Column 2, line 4) whereby their analog probe arrays optimize hybridization (Column 1, lines 52-58). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probes of Wu et al by attaching them to beads and/or microarrays as taught by McGall for the expected benefit of optimizing probe-target hybridization as taught by McGall (Column 1, lines 52-58).

Regarding Claim 16, Wu et al disclose a method for assessing the presence of a target comprising providing a solid support having a surface area and probes comprising analogs capable of fluorescence (Column 4, lines 28-61), detecting a first level of fluorescence, applying a sample comprising unlabeled target molecules, providing hybridization conditions, detecting the second level of fluorescence, comparing the first and second levels of fluorescence and identifying probe-target hybridization as the level of fluorescence approaches zero i.e. decreases by quenching (Column 7, lines 23-41 and Column 8, lines 8-19). Wu et al is silent regarding the solid support being a microarray having quadrants.

However, microarrays having quadrants and quadrant detection were well known in the art at the time the claimed invention was made as taught by McGall et al (Column 1, line 59-Column 2, line 4 and Fig. 1) whereby their analog probe arrays optimize hybridization (Column 1, lines 52-58). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probes of Wu et al by attaching them to beads and/or microarrays as taught by McGall for the expected benefit of optimizing probe-target hybridization as taught by McGall (Column 1, lines 52-58).

Regarding Claim 17, Wu et al disclose a method for quantifying the amount of a target comprising providing a substrate having a surface area comprising a known number of labeled

probes (Column 7, lines 25-28) including at least one analog capable of fluorescence (Column 4, lines 28-61), detecting a first level of fluorescence, contacting the substrate with a sample containing unlabeled target molecules, providing hybridization conditions, detecting the second level of fluorescence, comparing the first and second levels of fluorescence and identifying probe-target hybridization as the level of fluorescence approaches zero i.e. decreases by quenching (Column 7, lines 23-41 and Column 8, lines 8-19). Wu et al is silent regarding removing the substrate and repeating the steps with subsequent substrate to thereby calculate the amount of target. However, McGall et al teach a similar method wherein the substrate is removed to detect fluorescence and repeating with subsequent substrates to thereby compare hybridizations between differing probes (Example 6, Column 20, line 38-Column 21, line 8). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Wu et al by detecting fluorescence from subsequent substrates as taught by McGall et al for the expected benefit of providing a comparison of hybridizations between differing probes as taught by McGall et al (Example 6, Column 20, line 38-Column 21, line 8).

Regarding Claim 20, Wu et al disclose a method for quantifying the amount of a target comprising incorporating fluorescent nucleotide analogs into probes(Column 4, lines 28-61), detecting a first level of fluorescence, hybridizing a target with the probes to form probe-target complex, detecting the second level of fluorescence, comparing the first and second levels of fluorescence and identifying probe-target hybridization as the level of fluorescence approaches zero i.e. decreases by quenching (Column 7, lines 23-41 and Column 8, lines 8-19). Wu et al is silent regarding a washing step. However, McGall et al teach the similar method comprising a wash step whereby stringency is reduced and/or increased according to experimental design (Column 20, lines 57-65). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Wu et al

by including the wash step of McGall et al for the expected benefit of providing the desired stringency as taught by McGall et al (Column 20, lines 57-65).

10. Claims 14-15 rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al U.S. Patent No. 5,846,729, issued 8 December 1998) in view of Hornes et al (U.S. Patent No. 5,512,439, issued 30 April 1996).

Regarding Claims 14-15, Wu et al disclose the substrate of Claim 1 having a surface area comprising attached labeled probe molecules, said labeled probes having incorporated therein nucleotide analogs that fluoresce (Column 4, lines 28-45) and whose decrease in fluorescence quantifies the presence or hybridization of complementary molecules by quenching a first fluorescence provided by the labeled probes (Column 4, lines 45-61 and Column 8, lines 7-19). Wu et al teach the substrate is a solid support (Column 8, line 7) but they are silent regarding the support being a bead of a ferromagnetic core (Claim 14) or having 100 to 1,000 labeled probes attached (Claim 15).

However, ferromagnetic beads having 100 to 1,000 labeled probes attached were well known in the art at the time the claimed invention was made as taught by Hornes et al (Column 5, lines 11-20). Hornes et al further teach that their ferromagnetic beads "ensure" rapid and uniform reaction kinetics (Column 2, lines 47-56). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the solid support of Wu et al by utilizing the ferromagnetic beads having 100 to 1,000 labeled probes

attached for the expected benefit of rapid and uniform reaction kinetics as taught by Hornes et al (Column 2, lines 47-56).

11. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al U.S. Patent No. 5,846,729, issued 8 December 1998) in view of McGall et al (U.S. Patent No. 6,156,501, filed 3 April 1996) as applied to Claim 17 above and further in view of Vyas et al (U.S. Patent No. 5,776,711, issued 7 July 1998).

The limitations of Claim 17 are taught by Wu et al and McGall et al and are addressed above.

Regarding Claim 18, Wu et al disclose the method of Claim 17 wherein the probes are affixed on a solid support Column 8, lines 8-19) and McGall et al teach the similar method wherein the solid support is a bead (Column 2, lines 5-11). Wu et al and McGall et al are silent regarding detecting labels using a flow cytometer.

However, flow cytometer label detection was well known in the art at the time the claimed invention was made as taught by Vyas et al (Abstract). Furthermore, Vyas et al teach that flow cytometer detection is preferred bead-immobilized complexes because the flow cytometer provides for simultaneous detection of multiple analytes (Column 7, lines 47-53). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the label detection of Wu et al and McGall by using the flow cytometer for the expected benefit of detecting multiple analytes simultaneously as taught by Vyas et al (Column 7, lines 47-53).

12. Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al U.S. Patent No. 5,846,729, issued 8 December 1998) as defined by Egholm et al (Nature, 7 October 1993, 365: 566-568) in view of McGall et al (U.S. Patent No. 6,156,501, filed 3 April 1996).

Regarding Claim 40, Wu et al disclose a method for quantifying the amount of a target comprising incorporating fluorescent nucleotide analogs into probes (Column 4, lines 28-61), detecting a first level of fluorescence, hybridizing a target with the probes to form probe-target complex, detecting the second level of fluorescence, comparing the first and second levels of fluorescence and identifying probe-target hybridization as the level of fluorescence approaches zero i.e. decreases by quenching wherein the labeled probe is affixed on a substrate (Column 7, lines 23-41 and Column 8, lines 8-19).

Furthermore, Wu et al teach the probes comprise PNA nucleotide analogs as described by Egholm et al (Column 4, lines 19-25). Egholm teaches that PNA nucleotide analogs are 2-amino purine (Abstract). Therefore, the PNA nucleotide analogs of Wu et al are 2-amino purines as claimed.

Wu et al is silent regarding a washing step. However, McGall et al teach the similar method comprising a wash step whereby stringency is reduced and/or increased according to experimental design (Column 20, lines 57-65). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Wu et al by including the wash step of McGall et al for the expected benefit of providing the desired stringency as taught by McGall et al (Column 20, lines 57-65).

13. Applicant's amendment to the specification necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878 until 13 January 2004. Starting 14 January 2004, the examiner's phone number will be (517) 272-0741. The examiner can normally be reached on 6:00 TO 3:30 Monday through Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
December 3, 2003